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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,729	MCWILLIAMS ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *8-17 and 25-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2003 and 2/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-7 and 18-24 in the reply filed on October 15, 2004 is acknowledged. The traversal is on the ground(s) that "[A]pplicants elect with traverse because simultaneous examination of the inventions does not impose an undue burden of examination on the Examiner" .

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that Groups I to V will be examined. First, in previous restriction, the examiner has clearly indicated why the restriction was made. Specially, the examiner clearly indicated that there were burdens to search Groups I, III and V together, Groups II, III, IV, and V together, Groups III, IV, and V together. Second, applicant does not explain why simultaneous examination of the inventions does not impose an undue burden of examination on the Examiner. Therefore, the requirement is still deemed proper and is therefore made FINAL and claims 1-7 and 18-24 will be examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 3, 5, 7, 18, 20, and 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 when a complex biological construct contains genetic materials (DNA or/and RNA), does not reasonably provide enablement for performing the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 when a complex biological construct does not contain genetic materials (DNA or/and RNA). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to perform the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 when a complex biological construct does not contain genetic materials (DNA or/and RNA). While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 can be performed when a complex biological construct does not contain genetic materials (DNA or/and RNA).

Claims 1, 3, 18, and 20 require to determine gene expression and isolate genetic molecules. Since there is no definition for "a complex biological construct" in the specification, "a complex biological construct" recited in claims 1, 3, 18, and 20 can be interpreted as a biological complex containing DNA/RNA or a biological complex without DNA/RNA such as a biological complex formed by different carbohydrates, lipids and proteins. When a biological complex recited in claims 1, 3, 18, and 20 does not contain DNA/RNA (i.e., a biological complex formed by different carbohydrates, lipids and proteins), it is impossible to perform the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 and the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 are unpredictable.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes to test whether the methods recited in claims 1, 3, 5, 7, 18, 20, and 22-24 can be performed when a biological complex recited in claims 1, 3, 18, and 20 does not contain DNA/RNA (i.e., a biological complex formed by different carbohydrates, lipids and proteins).

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-7 and 18-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1 and 18 recite the limitation "said solution" in the claims. There is insufficient antecedent basis for this limitation in the claims because there is no word "solution" in liquefying step. Please clarify.

7. Claims 1 and 18 are rejected as vague and indefinite. Although the claims require determining gene expression, it is unclear that what kind of gene expression is determined since there is no nucleic acid in the claim. Please clarify.

8. Claims 3 and 20 recite the limitation "isolating genetic molecules" in the claims. There is insufficient antecedent basis for this limitation in the claims because the claims do not require that a complex biological construct must contain genetic molecules. Please clarify.

9. Claim 3 is rejected as vague and indefinite. Although claim 3 is directed to a method of analyzing genetic expression, there is no step for analyzing genetic expression in the content of the claim and the goal (see preamble) cannot reach. Please clarify.

10. Claims 4 and 21 recite the limitation "the cells of said complex biological component" in the claims. There is insufficient antecedent basis for this limitation in the claims because a complex biological construct recited in claims 3 and 20 does not contain cells and "said complex biological construct" recited in claims 3 and 20 and "the cells of said complex biological component" recited in claims 4 and 21 are not equal. Please clarify.

11. Claim 6 recited the limitation "said gene expression analysis" in the claims. There is insufficient antecedent basis for this limitation in the claims because "analyzing genetic expression" is only found in the preamble of the claim and is not found in the content of the claim, and "gene expression analysis" and "analyzing genetic expression" are not the same wording. Please clarify.

12. Claim 23 recited the limitation "said gene expression analysis" in the claims. There is insufficient antecedent basis for this limitation in the claims because "analyzing of genetic expression" is only found in the preamble of the claim and is not found in the content of the claim, and "gene expression analysis" and "analyzing of genetic expression" are not the same wording. Please clarify.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Lockhart *et al.*, (US Patent No. 6,524,800 B2, filed on July 6, 2001).

Regarding claim 1, since Lockhart *et al.*, teach to prepare RNA sample from tissue samples using an acid guanidinium-phenol-chloroform extraction method (see columns 11 and 12) and the process of prepare RNA sample must include liquefying the tissue samples, Lockhart *et al.*, disclose liquefying a complex biological construct (ie., tissue samples) as recited in claim 1. Since Lockhart *et al.*, teach a method for massive parallel gene expression monitoring comprising: (a) providing a pool of target nucleic acids comprising RNA transcript(s) of one or

more target gene(s); (b) hybridizing the nucleic acid sample to a high density array of probes; and (c) detecting the hybridized nucleic acids and calculating a relative and/or absolute expression (transcription, RNA processing or degradation) level (see column 11, third and fourth paragraphs), Lockhart *et al.*, disclose transferring said solution (ie., RNA sample in a solution) to a microarray and determining gene expression as recited in claim 1.

Regarding claim 18, since Lockhart *et al.*, teach to prepare RNA sample from tissue samples using an acid guanidinium-phenol-chloroform extraction method (see columns 11 and 12) and the process of prepare RNA sample must include liquefying the tissue samples, Lockhart *et al.*, disclose liquefying a complex biological construct (ie., tissue samples) into a solution having complete and uncontaminated genetic molecules (ie., RNA sample) as recited in claim 1. Since Lockhart *et al.*, teach a method for massive parallel gene expression monitoring comprising: (a) providing a pool of target nucleic acids comprising RNA transcript(s) of one or more target gene(s); (b) hybridizing the nucleic acid sample to a high density array of probes; and (c) detecting the hybridized nucleic acids and calculating a relative and/or absolute expression (transcription, RNA processing or degradation) level (see column 11, third and fourth paragraphs), Lockhart *et al.*, disclose transferring said solution (ie., RNA sample in a solution) to a microarray and determining gene expression as recited in claim 1.

Therefore, Lockhart *et al.*, teach all limitations recited in claims 1 and 18.

15. Claims 3, 4, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Sambrook *et al.*, (Molecular Cloning: A laboratory Manual, second edition, 7.18-7.22, 1989).

Regarding claims 3, 4, 20, and 21, since Sambrook *et al.*, teach to mix 5 volume of guanidinium thiocyanate homogenization buffer with a fragment of tissue and homogenize the cell lysates with a grinder or homogenizer (see 7.19), Lockhart *et al.*, disclose placing a complex biological construct (ie., tissue samples) into a chamber (ie., a container with mixture of guanidinium thiocyanate and a fragment of tissue) and liquefying said complex biological construct in said chamber wherein a solution is formed as recited in claims 1and 20 and further comprising the step of inserting a component (ie., a grinder or homogenizer) into said chamber wherein said component ruptures the cells of said complex biological component as recited in claims 4 and 21. Since Sambrook *et al.*, teach to transfer supernatant of a mixture of homogenization after centrifugation into a fresh tube and isolate RNA by CsCl gradient (see 7.20-7.22), Sambrook *et al.*, disclose removing said solution from said chamber (ie., a container with mixture of guanidinium thiocyanate and a fragment of tissue) and purifying said solution and extracting and isolating genetic molecules as recited in claims 3 and 20.

Therefore, Sambrook *et al.*, teach all limitations recited in claims 3, 4, 20, and 21.

16. Claims 3-7 and 20-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Lockhart *et al.*, (July 6, 2001) as evidence by Sambrook *et al.*, (Molecular Cloning: A laboratory Manual, second edition, 7.18-7.22, 1989).

Regarding claims 3, 4, 20, and 21, since Lockhart *et al.*, teach to prepare RNA sample From tissue samples using an acid guanidinium-phenol-chloroform extraction method published by Sambrook *et al.*, (see columns 11 and 12) and Sambrook *et al.*, teach to mix 5 volume of guanidinium thiocyanate homogenization buffer with a fragment of tissue and homogenize the

cell lysates with a grinder or homogenizer (see 7.19), Lockhart *et al.*, disclose placing a complex biological construct (ie., tissue samples) into a chamber (ie., a container with mixture of guanidinium thiocyanate and a fragment of tissue) and liquefying said complex biological construct in said chamber wherein a solution is formed as recited in claims 1 and 20 and further comprising the step of inserting a component (i.e., a grinder or homogenizer) into said chamber wherein said component ruptures the cells of said complex biological component as recited in claims 4 and 21. Since Sambrook *et al.*, teach to transfer supernatant of a mixture of homogenization after centrifugation into a fresh tube and isolate RNA by CsCl gradient (see 7.20-7.22), Sambrook *et al.*, disclose removing said solution from said chamber (ie., a container with mixture of guanidinium thiocyanate and a fragment of tissue) and purifying said solution and extracting and isolating genetic molecules as recited in claims 3 and 20.

Regarding claims 5 and 22, since Lockhart *et al.*, teach to prepare a high density assay having a plurality of oligonucleotides for gene expression monitoring (see columns 14-18), Lockhart *et al.*, disclose preparing gene expression analysis as recited in claims 5 and 22.

Regarding claims 6 and 23, since Lockhart *et al.*, teach that compound 52 and flavipiridol increase gene expression of certain genes (see Figure 3A and column 2), Lockhart *et al.*, disclose said gene expression analysis includes an analysis of gene function (ie., certain genes response to treatment of compound 52 and flavipiridol) as recited in claims 6 and 23.

Regarding claims 7 and 24, since the high density assay taught by Lockhart *et al.*, has a plurality of oligonucleotides (see column 15, last paragraph) and total RNA used for hybridization taught by Lockhart *et al.*, have thousands of different mRNAs encoding thousands of corresponding known and unknown genes, Lockhart *et al.*, teach that genetic molecules (ie., a

plurality of oligonucleotides) are placed in a microarray for matching known and unknown genetic molecules (ie., thousands of different mRNAs in total RNA used for hybridization taught by Lockhart *et al.*,) as recited in claims 7 and 24.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 2 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart *et al.*, (July 6, 2001) as applied to claims 1 and 18 above, and further in view of Pittman *et al.*, (US 2003/0154032 A1, priority date: December 15, 2000).

The teachings of Lockhart *et al.*, have been summarized previously, *supra.*

Lockhart *et al.*, do not disclose that the complex biological construct is a gross

anatomical structure of an animal comprising more than one type of tissue as recited in claims 2 and 19.

Pittman *et al.*, teach to isolate total RNA from mouse paws (see column 33, [0330]). Mouse paw is considered as complex biological construct with a gross anatomical structure of an animal comprising more than one type of tissue.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claims 2 and 19 wherein the complex biological construct is a gross anatomical structure of an animal comprising more than one type of tissue in view of the patents of Lockhart *et al.*, and Pittman *et al.*, One having ordinary skill in the art would have motivated to do because the simple replacement of one kind of the complex biological construct (i.e., tissue samples taught by Lockhart *et al.*,) from another kind of the complex biological construct (i.e., mouse paws taught by Pittman *et al.*,) as a starting material during the process for performing the method recited in claims 2 and 19 would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

19. No claim is allowed.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
January 6, 2005

FRANK LU
PATENT EXAMINER